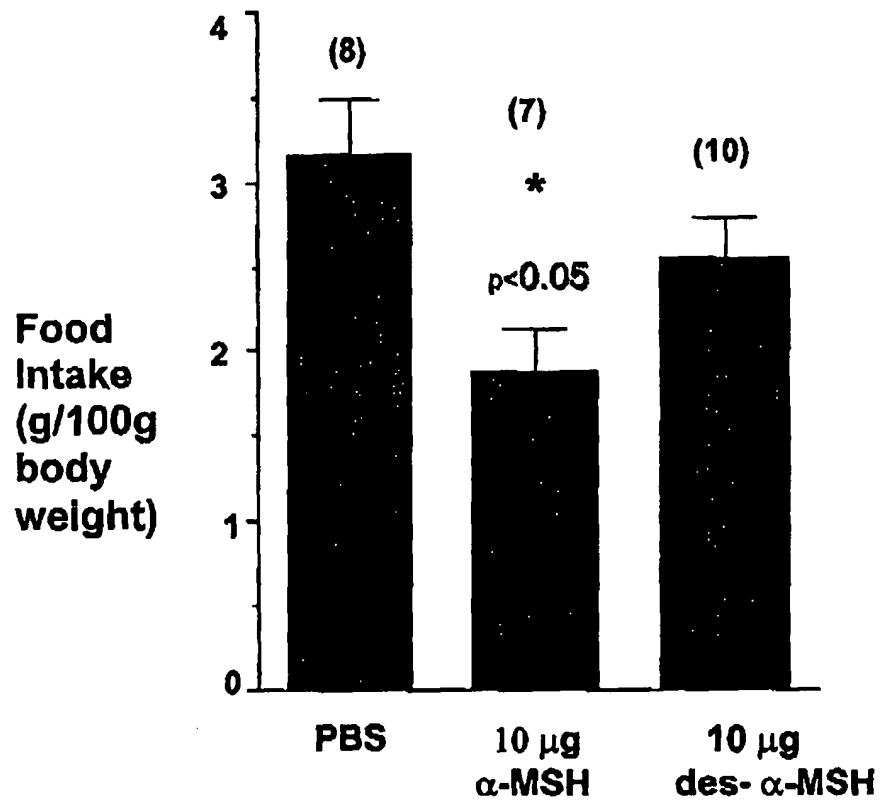
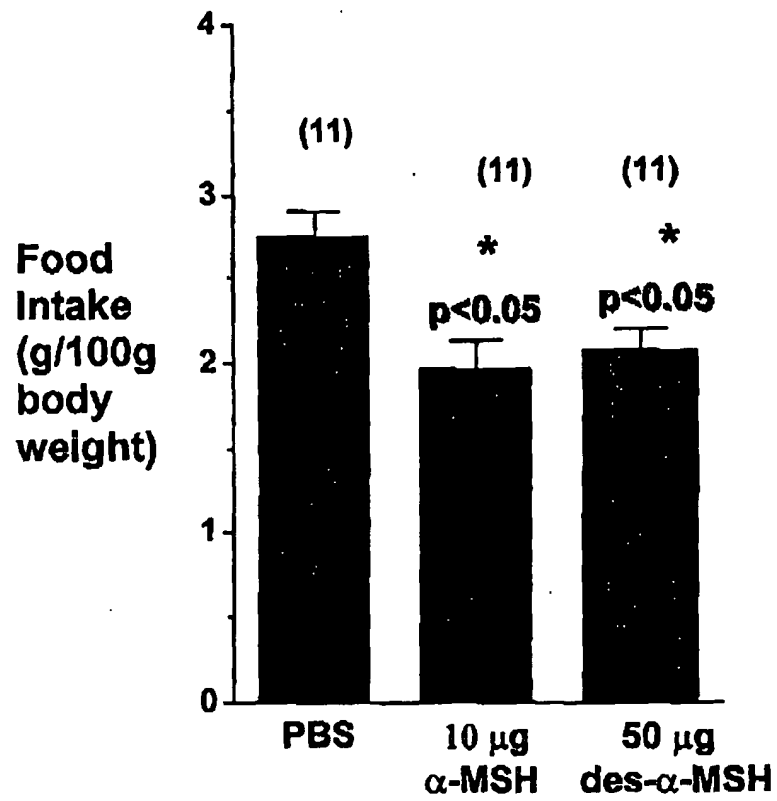
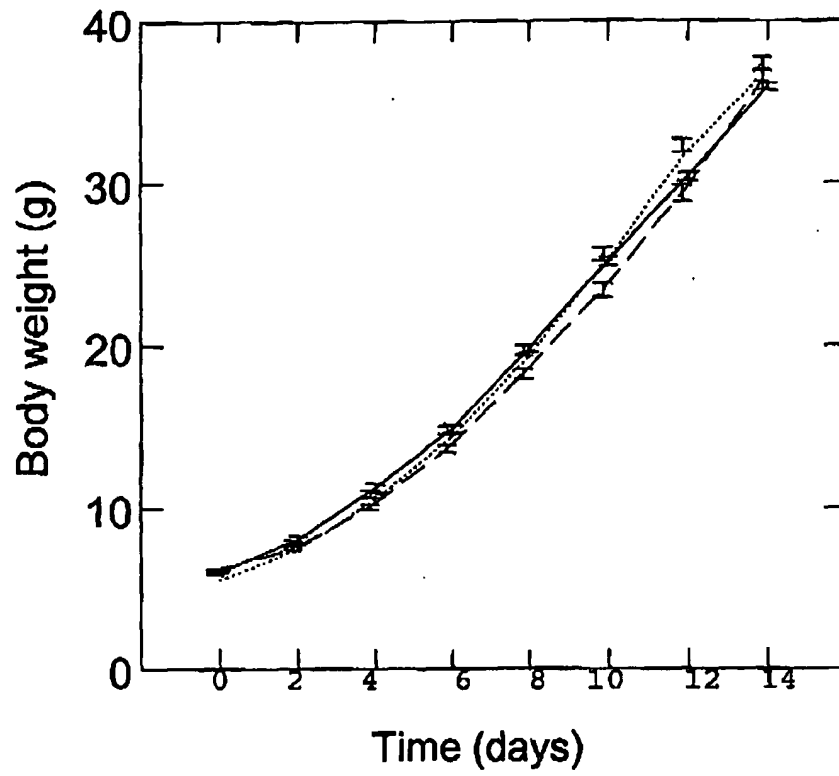


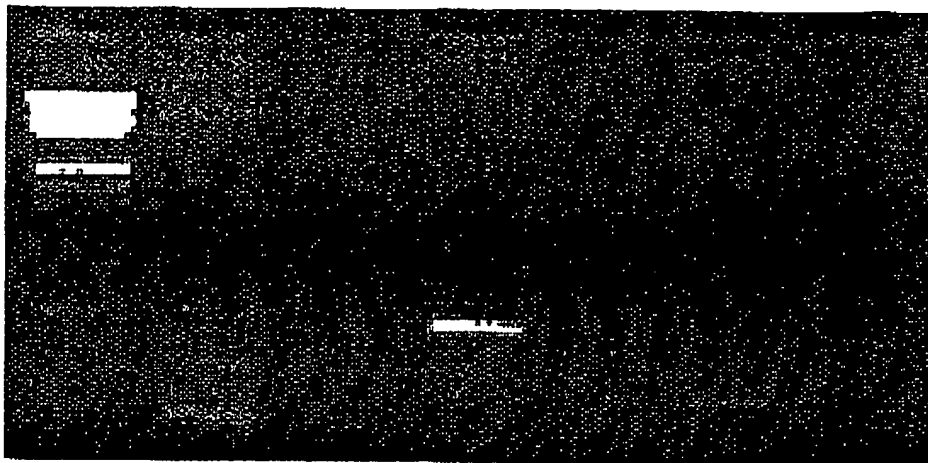
FIGURE 1

**Figure 2**

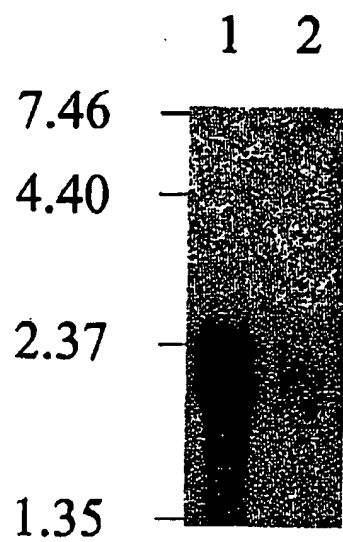
**Figure 3**

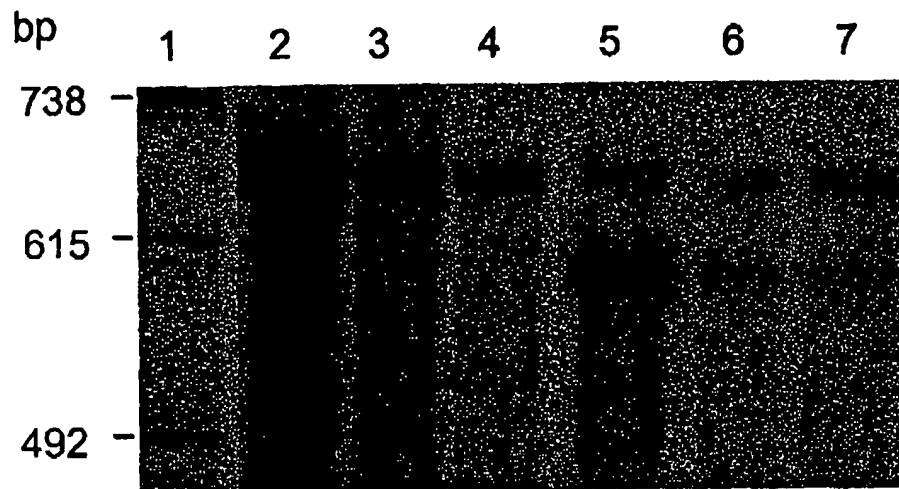
**Figure 4**

564  
bp



**Figure 5**

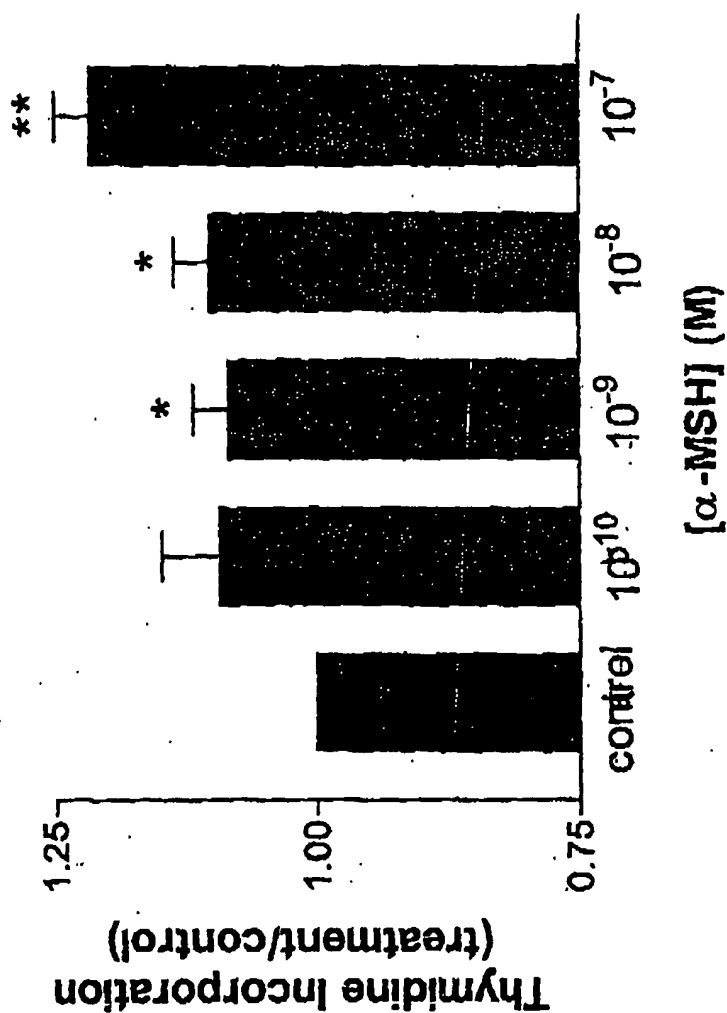
**Figure 6**



**Figure 7**

FIG 8.

**Effects of  $\alpha$ -MSH on  
Thymidine incorporation in  
Osteoblasts**



\*=significantly different from control ( $p < 0.04$ )

\*\*=significantly different from control ( $p < 0.001$ )



9/15

## Des-acetyl $\alpha$ -MSH is Antagonistic to $\alpha$ -MSH in Osteoblasts

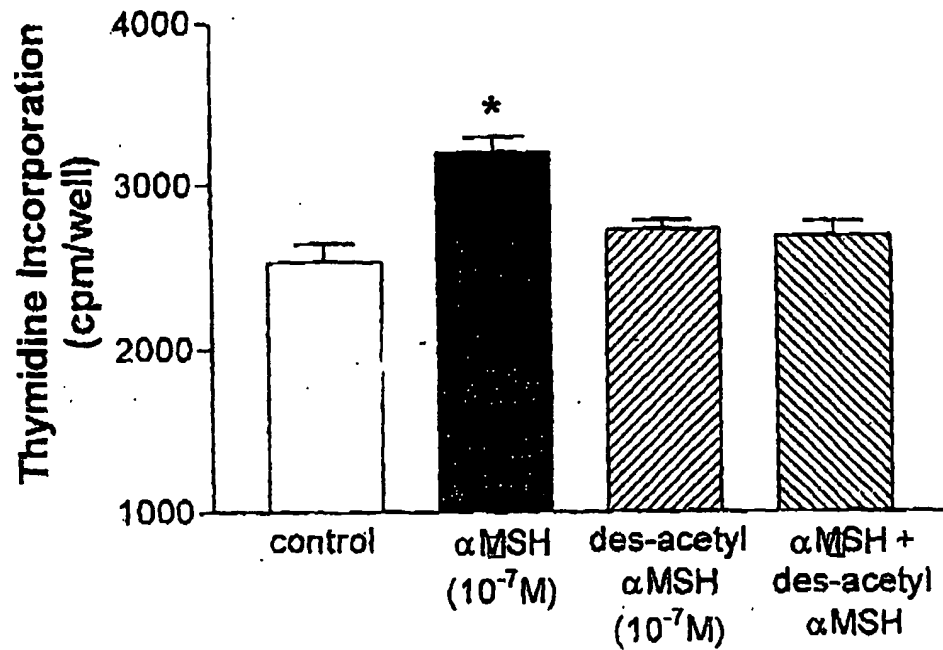
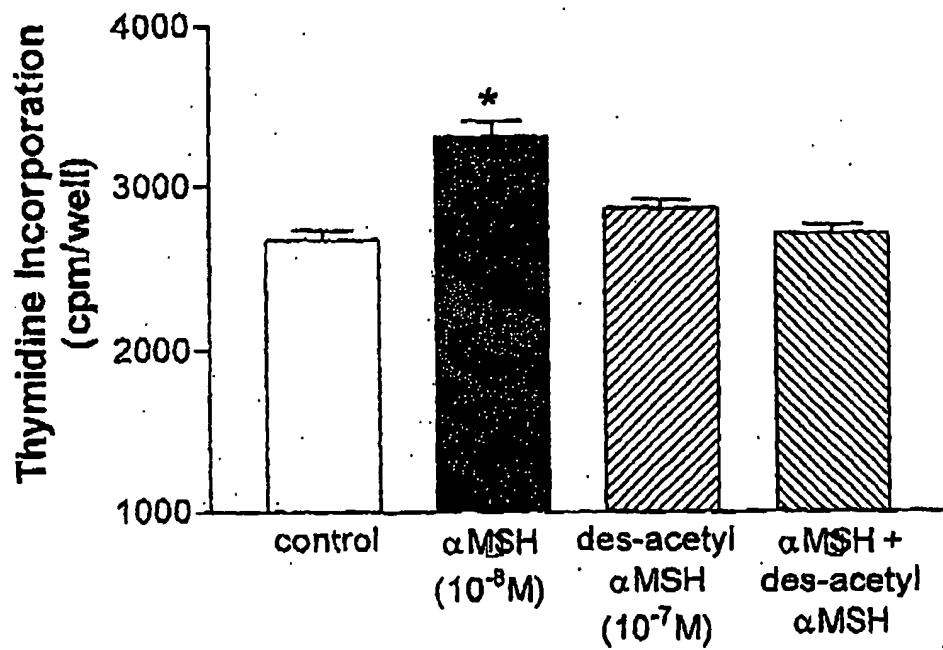
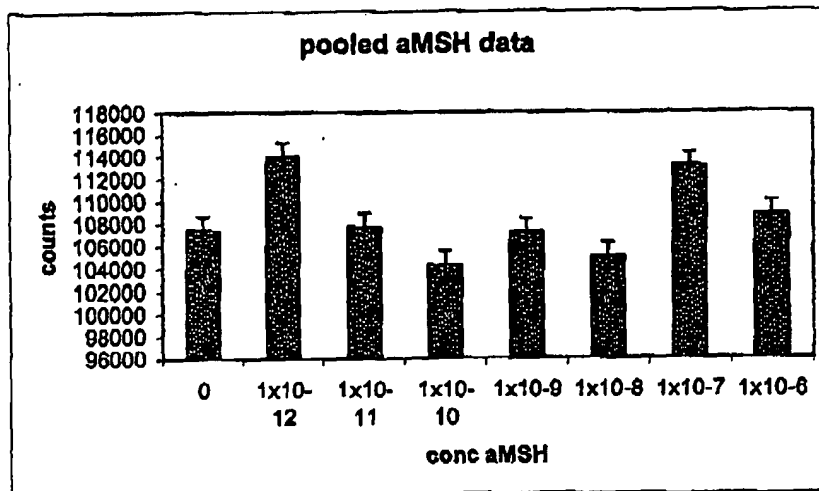
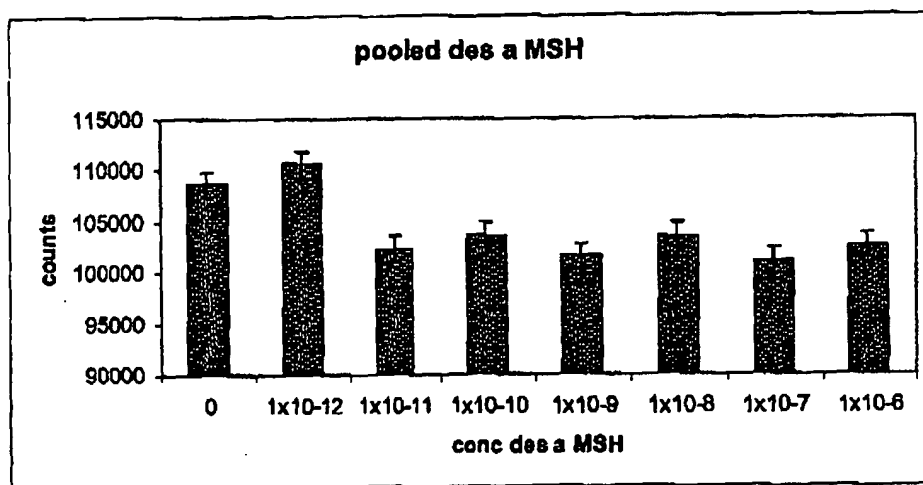


FIG 9



**Figure 10**



**Figure 11**

# Examples of proteins identified

WO 03/104761

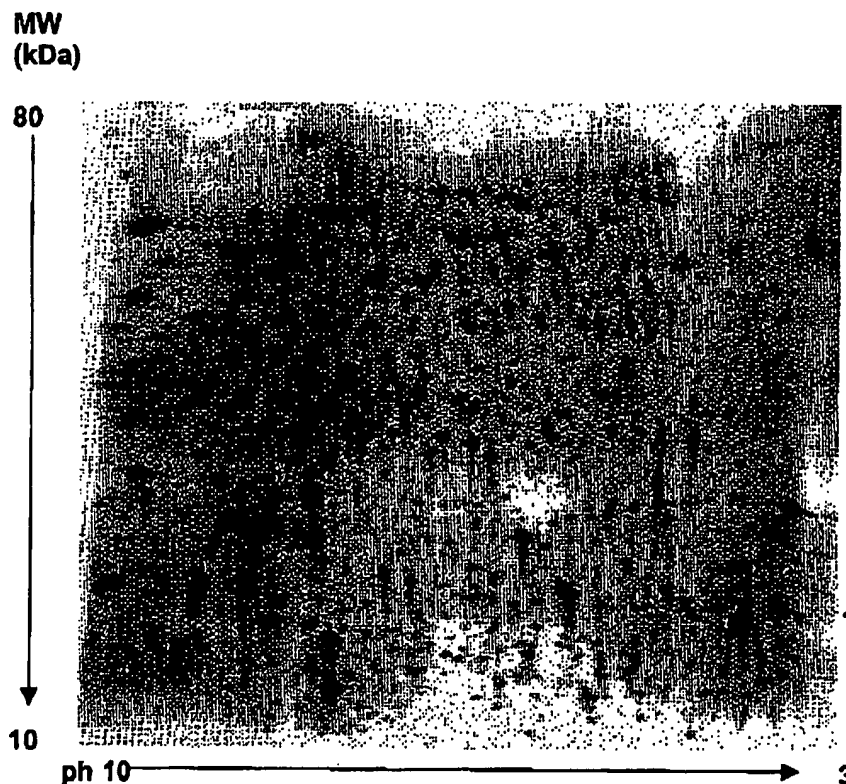
12/15

PCT/IB03/02641

07/217684

Protein	Spot no. (Fig 3,4)	$\alpha$ -MSH effect compared to control	des- $\alpha$ -MSH effect compared to control
<b>Stress protein</b>			
heat shock protein homologue	p1350 (3)	1.8 fold increase	
<b>Enzymes</b>			
Glyceraldehyde-3-phosphate-dehydrogenase	p1528 (3)	*	
	p582 (4)		
	p1210 (4)		2.4 fold decrease
	p582 (4)		*
	p582 (4)		*
aldo-keto reductase	p706 (3)	1.7 fold increase	
citrate synthase	p86 (4)		
creatine kinase	p1528 (3)		1.6 fold decrease
pyruvate synthase alpha-chain			
f1 ATPase beta-chain			
<b>Cytoskeletal proteins</b>			
tubulin beta chain	p711 (3)	1.4 fold increase	

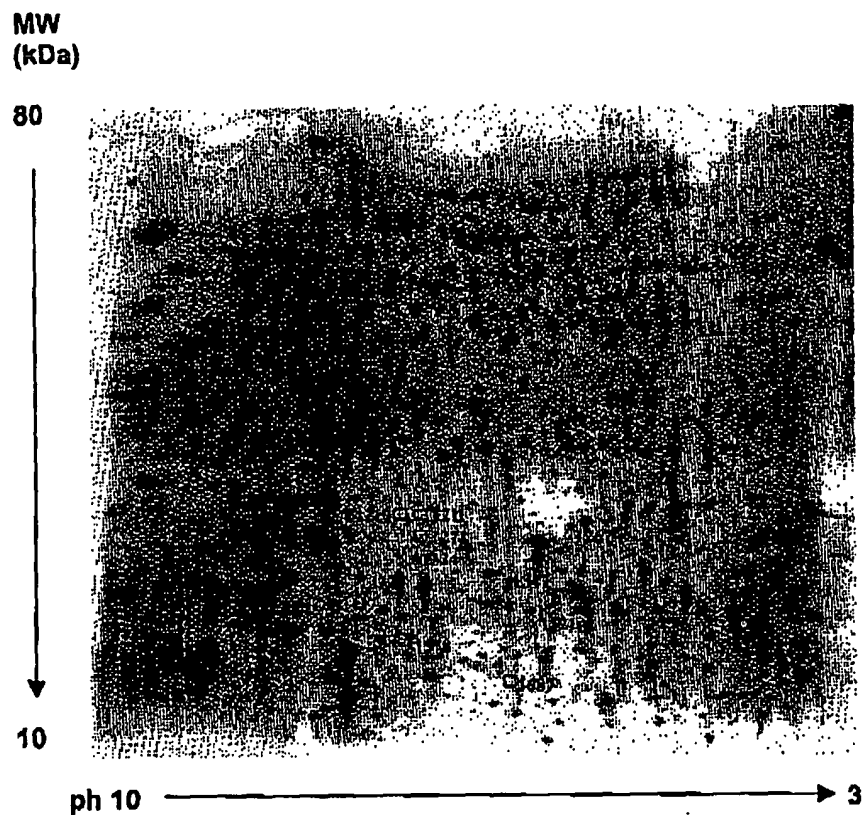
\* Multiple proteins that appeared as a single spot on the 2D gel.



### Proteins changed by $\alpha$ -MSH

**treatment** Location of proteins of interest (black-circles) on the reference gel. Numbers correspond to protein labels on the reference gel. Significant increase ( $p < 0.05$ , Mann-Whitney U test) in protein expression in  $\alpha$ -MSH treated group is labeled in blue, decrease in red. Underlined protein p611 expression also significantly changed in des- $\alpha$ -MSH treated group.

**Figure 12B**



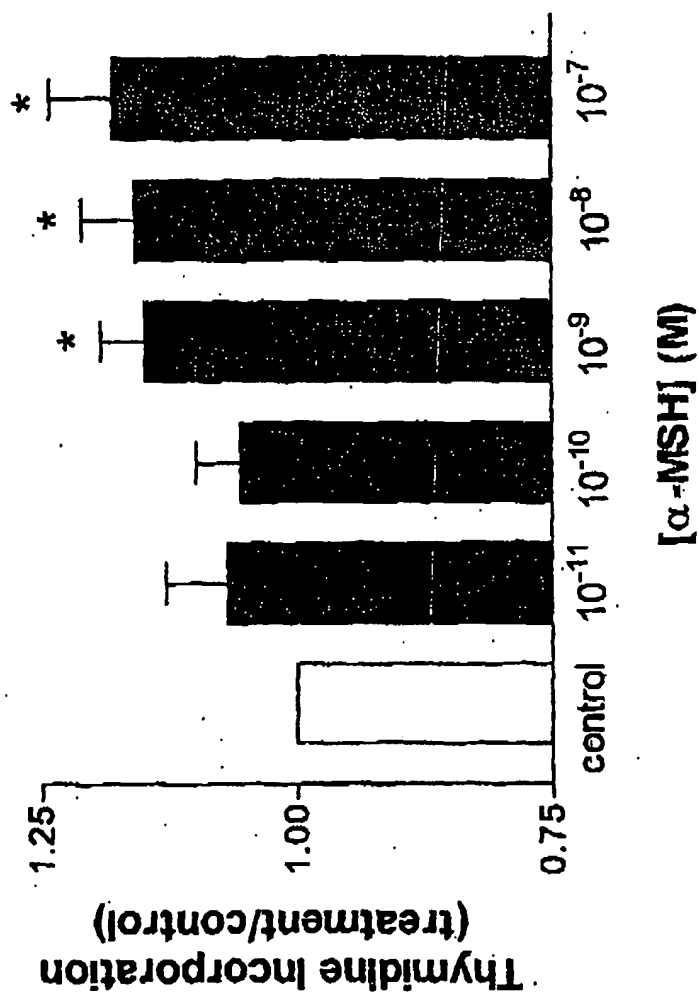
### Proteins changed by des- $\alpha$ -MSH

**treatment** Location of proteins of interest (black-squares) on the reference gel. Numbers correspond to protein labels on the reference gel. Significant increase ( $p < 0.05$ , Mann-Whitney U test) in protein expression in des- $\alpha$ -MSH treated group is labeled in blue, decrease in red. Underlined protein p611 expression also significantly changed in  $\alpha$ -MSH treated group.

**Figure 12C**

FIG. 13.

**Effects of  $\alpha$ -MSH on Thymidine  
Incorporation in Chondrocyte Monolayers**



\*=significantly different from control ( $p < 0.03$ )

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

**BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☒ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**